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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/581,094

08/28/2008

Mats Ranby

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ALEXANDRIA, VA 22314-1176

EXAMINER

SHEN, BIN

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/581,094	Applicant(s) RANBY, MATS	
	Examiner BIN SHEN	Art Unit 1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 July 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 7-17 is/are pending in the application.
- 4a) Of the above claim(s) 16 and 17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 7-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>5/31/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The IDS received 5/31/2006, the preliminary amendment received 5/31/2006 have been entered.

Election

Applicant's election of group I, claims 1-4, 7-15 in the reply filed on 7/12/2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election **without traverse** (MPEP § 818.03(a)).

Claims 16, 17 are non-elected, thus are withdrawn from further examination. Only claims 1-4, 7-15 are presented for examination on the merits.

Benefit of priority is to 12/2/2003.

Specification

The abstract of the disclosure is objected to because the abstract must be a single paragraph. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

This application does not contain an abstract of the disclosure as required by 37 CFR 1.772(b). An abstract on a separate sheet is required to replace the provided abstract of the WO file front of the parent PCT.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite by the phrase “determine an analyte concentration of an anticoagulated plasma by....on a mixture of a blood” (lines 1-3 and lines 6-7). It is unclear what is determined here, if the analyte is in the plasma or blood or both, and what kind of blood sample “corresponding to said anticoagulated plasma”, does blood sample treated with anticoagulant qualifies as blood sample “corresponding to said anticoagulated plasma”? It is confusing in step b) one measurement correlates with the hematocrit (line 9), but in the computing step “value of the hematocrit” is known (lines 14-15). Therefore, it is unclear how the analyte concentration is determined and what role hematocrit plays for determining analyte concentration.

Claim 2 is rendered vague and indefinite by the phrases “the volume of blood in....the volume of blood” in step a) and “the volume of reagentthe volume of reagent” in step b). How is "the volume of blood" defined by "the volume of blood", and “the volume of reagent” defined by “the volume of reagent”?

Claim 10 is rendered vague and indefinite by the word “analyte”. How can analyte be time (PT, APTT, ACT)?

Claim 14 is rendered vague and indefinite by the word “INR”. Please spell out at least at the first occurrence. It is also unclear how the analyte concentration is re-expressed in PT% prior to determination of analyte concentration because PT is measured to indicate analyte concentration.

Claim 1 recites the limitation "the precise correspondence" in lines 12-13. There is insufficient antecedent basis for this limitation in the claim.

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Claims 1 (in line 14), 2 (in lines 3, 5), 3 (in lines 2-3) recite the limitation "the test protocol". There is insufficient antecedent basis for this limitation in claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 7-10, 12, 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Owren (1959).

Owren teaches a method of determining concentration of four coagulation factors in citrated blood sample by measuring clotting-time using "all-in-one-reagent" (page 754, right column, 3rd paragraph), by mixing 0.1 ml citrated blood (page 755, right column, 4th full paragraph, lines 6-7) with 0.5 ml reagent (contains cephalin, the thromboplastin and all clotting factors which are not influenced by anti-coagulant treatment, page 754, right column, 3rd paragraph), and measuring coagulation-time (page 755, right column, 4th full paragraph, line 8), using normal known hematocrit value (page 756, left column, 2nd paragraph, line 5) to computing coagulant factor concentration (page 757, right column, Fig. 12); the anticoagulant used in the blood sample is sodium citrate (page 755, right column, 3rd paragraph, line 1); and the anticoagulated plasma is a fluid from citrated plasma (page 755, right column, 4th paragraph, line 6), the hemoglobin concentration is calibrated with known concentration in the corresponding citrated plasma (page 755, left column, Fig. 3); the concentration of coagulation factors corresponding to coagulation-time (page 754, Fig. 2) that read as activated clotting time (ACT). The reaction of the measurement is performed at 37°C (page 755, right column, line 5), thus the clotting time correlates with analyte concentration (page 754, right column, 3rd paragraph, line 8).

The method of **claim 1** is anticipated by Owren et al. because the method taught in Owren et al. comprises mixing 0.1 ml blood treated with anticoagulant citrate (and therefore

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anticoagulated plasma) with five fold 0.5 ml "all-in –one-reagent" (contains cephalin, the thromboplastin and all clotting factors which are not influenced by anti-coagulant treatment), and measuring coagulation time as correlate to analyte concentration and measuring normal hematocrit, then calculating or computing the analyte concentration by using normal hematocrit value. Because the test protocol is unknown, the blood volume is within 50-150% of the blood volume of the test protocol, the reagent volume is within 70-120% of the reagent volume of the test protocol, and the computation was determined when the hematocrit was known (**Claim 2**). Sodium citrate was used as the anticoagulant of the blood (**Claim 7**), and the plasma was derived from this citrated blood and is therefore citrated plasma (**Claim 8**). the analyte (coagulation factor) concentration is calibrated with known analyte concentration in the corresponding citrated plasma (**Claim 9**); the analyte-coagulation factor concentration corresponding to coagulation-time that read as activated clotting time (ACT, **Claim 10**); and the measurements are performed at 37°C (**Claim 12**); the clotting time measured correlates with coagulation factor concentration (**Claim 15**).

Claims 1, 2, 3, 4, 7-9, 12, 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Beresini (1993).

On page 2240, Fig. 2, Beresini teaches a method of quantification of analyte: cyclosporine (CsA) in citrated blood (abstract and page 2236, left column, lines 7-8) by mixing 36 µl pretreated citrated blood (page 2236, right column, 2nd full paragraph, lines 6-9) with 230 µl of reagents A and B at 37°C (page 2236, right column, 2nd full paragraph, line 6), and measuring CsA concentration (page 2237, Table 4), measuring hematocrit value (page 2238, left column, 1st full paragraph, lines 1-2) to study the effect of hematocrit on CsA concentration (page 2238, right column, lines 2-6); the anticoagulant used is sodium citrate (page 2236, left column, line 10), the CsA concentration is calibrated with known CsA concentration in the corresponding citrated plasma (page 2237, Table 4); and the CsA (analyte) concentration is shown on page 2240, Fig. 2.

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Therefore, Beresini anticipates the method of determining analyte (CsA) concentration from citrated blood sample (read as an anticoagulated plasma) by **a)** mixing 36 µl pretreated citrated blood with 230 µl of reagents A and B, and **b)** measuring CsA concentration, measuring hematocrit value to study the effect of hematocrit on CsA concentration (**Claim 1**); the volume of pretreated blood sample is 36 µl which is 100% of the volume of blood, the volume of reagents A and B together is 230 µl which is 100% of the volume of reagent, the result of the analyte concentration is shown on page 2240, Fig. 2 (**Claim 2**); therefore the volume of blood is 36 µl, the volume of reagent is 230 µl, (**Claim 3**), since the pretreated citrated blood was previously diluted twice (page 2236, right column, 1st full paragraph, lines 13-14) thus it also meet the limitation of **Claim 4** where the blood volume is 18 ul (36ul diluted twice), and reagent volume of 230 ul is in the range of 150 to 600 ul; wherein the anticoagulant used is sodium citrate (**Claim 7**); the anticoagulated plasma is a fluid derived from citrated plasma (**Claim 8**); the CsA concentration is calibrated with known CsA concentration in the corresponding citrated plasma (**Claim 9**); and the measurements are performed at 37°C (**Claim 12**); the correlations between CsA (analyte) concentration and the measurement (EMIT assay) is shown on page 2240, Fig. 2 (**Claim 15**).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Beresini and Zhang (2000).

Beresini teaches what is above as applied to claim 1.

Beresini does not teach hematocrit measurement of light with wavelengths in the range of 800 nm to 1100 nm (typical near-infrared range).

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Zhang teaches blood hematocrit measurement using near-infrared radiation that provide acceptable accuracy (page 295, left column, line 6, page 299, right column, end of 1st full paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Beresini to measure hematocrit with wavelengths in the range of 800 nm to 1100 nm (**Claim 11**) because Zhang the possibility and accuracy of measurement of hematocrit with near-infrared wavelength. One would have been motivated to make the modification because Beresini et al. specifically described a method of measuring analyte concentration with the measurement of hematocrit, and would reasonably have expected success in view of Zhang's teaching of using 800 nm to 1100 nm wavelength to measure hematocrit.

Claims 1, 13, 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Beresini and Potzsch (1997).

Beresini teaches what is above as applied to claims 1.

Beresini does not teach the reagent contains 0.1 g/L or more fibrinogen, the analyte concentration is expressed in INR.

Potzsch teaches a method of monitoring hirudin concentration (page 380, Fig.4) in citrated blood sample (page 375, line 3) by measuring snake venom enzyme ecarin clotting time (page 376, Table 1) expressed in INR (page 380, Fig. 4, **Claim 14**). The minimal concentration of fibrinogen for the assay is 50 mg/dl (**0.5 g/L**, page 376, 2nd paragraph, line 10, page 377, Fig. 1, **Claim 13**).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Beresini to use above minimal concentration of fibrinogen in the reagent (above 0.1g/L, **Claim 13**) to measure the concentration of different analyte and expressed the concentration in INR (**Claim 14**) because Potzsch teaches monitoring hirudin concentration by measuring snake venom enzyme ecarin clotting time expressed in INR with above minimal concentration of fibrinogen in the sample. One would have been motivated to make the modification because Beresini et al. specifically described a method of determining CsA concentration, and would reasonably have expected success in view of Potzsch's testing of

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the minimal concentration of fibrinogen in the sample and to express the analyte's concentration in INR..

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Bin Shen, whose telephone number is (571) 272-9040. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to her office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at (571) 272-0925.

B Shen

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/Karen Cochrane Carlson/

Primary Examiner, Art Unit 1656